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# Synthesis, Structure and Reactivity of an Evans-type Bis(imide) Derived From a $C_2$-Symmetric Bis(oxazolidinone). A Reluctant Chiral Auxiliary

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**Dedicated to Professor Göran Bergson on the occasion of his 65th birthday**

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This paper describes the enantiospecific synthesis of the $C_2$-symmetric bis(oxazolidinone) **9** from (−)-1,4-di-*O*-benzyl-L-threitol (**3**). Compound **9** was intended for use as a bifunctional chiral auxiliary in asymmetric alkylation and aldol reactions. However, in the presence of strong non-nucleophilic bases the bis(imide) derivative **10** (the structure of which has been studied in detail by means of NMR spectroscopy, X-ray crystallography and computational methods) did not react with external electrophiles. This lack of reactivity has been interpreted on the basis of a conformational analysis of **10**.

In the field of asymmetric synthesis via the use of recoverable chiral auxiliaries, the chiral oxazolidinones introduced and developed by Evans[1a–c] (e.g. **1** and **2**, Fig. 1) have proved to be remarkably efficient and versatile. These auxiliaries have been used for a variety of asymmetric transformations, including alkylations, aldol reactions, and Diels–Alder cycloadditions; diastereoselectivities of 95% or better seem to be the rule rather than the exception! Furthermore, the Evans group has made extensive use of this methodology in a number of total syntheses of highly complex natural products.[2]

More recently, the concept of bifunctional chiral auxiliaries has been exploited.[3] This technique relies on the use of a bifunctional $C_2$-symmetric auxiliary which allows for two diastereoselective reactions to occur, with the same sense of asymmetric induction, on a single substrate molecule; two molecules of enantiomerically enriched product can then be produced per molecule of auxiliary, as exemplified[3] in Scheme 1.

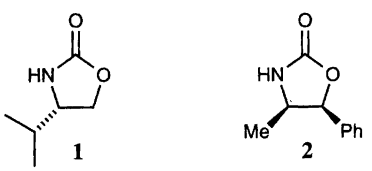


*Fig. 1.* Chiral oxazolidinone auxiliaries introduced by Evans.[1]

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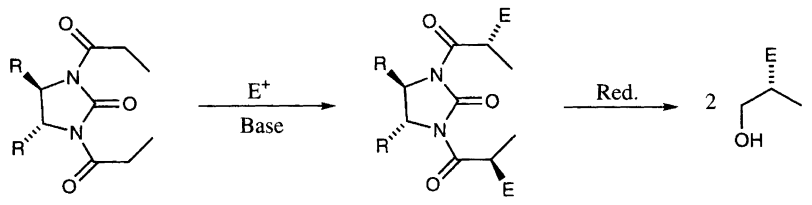
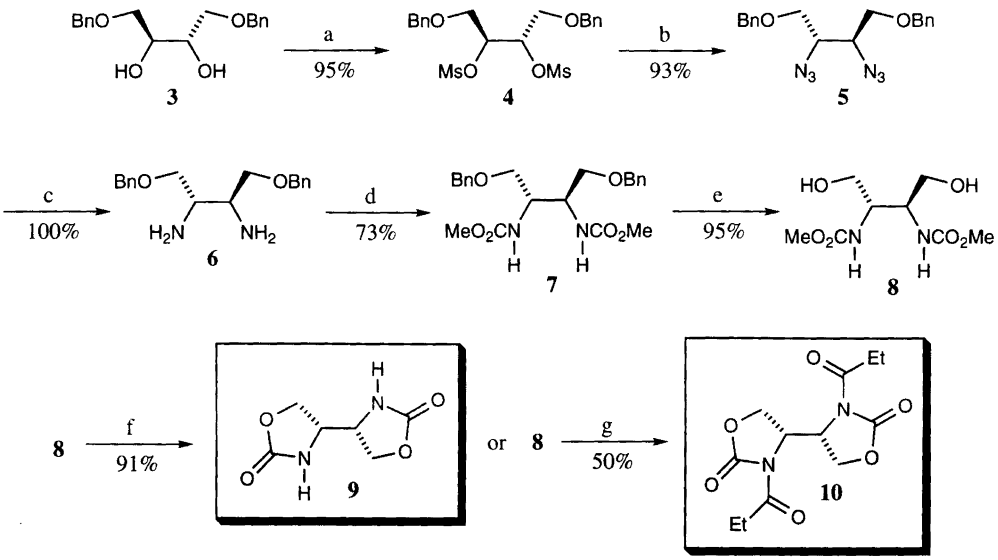
Intrigued by the concept of $C_2$-symmetry[4] as a control element in asymmetric synthesis, and impressed by the success of the Evans-type auxiliaries, we decided to prepare a bifunctional chiral auxiliary based on the oxazolidinone system. In our approach, the substituent on the oxazolidinone ring would thus be the oxazolidinone itself, and the first part of this paper describes the simple enantiospecific synthesis of the $C_2$-symmetric bis(oxazolidinone) **9** and its conversion into **10** (Scheme 2). The former was projected for use in a range of asymmetric syntheses *à la* Evans, and the latter was the substrate chosen for testing in asymmetric alkylation and aldol reactions. As will be seen, however, our plans were thwarted by the reluctance of **10** to undergo reaction under conditions typically used[1f,g] for Evans-type chemistry. We have studied the structure of **10** in some detail, by means of a combination of NMR spectroscopy, X-ray crystallography and computational chemistry, in an attempt to explain the frustrating behaviour of the bis(oxazolidinone).

## Results and discussion

*Enantiospecific synthesis of bis(oxazolidinones)* **9** *and* **10**. The starting material chosen (Scheme 2) was (−)-1,4-di-



*Scheme 1.* Use of a $C_2$-symmetric bifunctional chiral auxiliary according to Davies.[3]



*Scheme 2.* (a) MsCl, pyridine; (b) $NaN_3$, DMF; (c) $H_2$, Pd–C, MeOH; (d) methyl chloroformate, NaOH, MeOH; (e) $H_2$, $Pd(OH)_2$–C, MeOH; (f) NaH, DME; (g) NaH, DME then propionyl chloride.

*O*-benzyl-L-threitol (**3**) which is commercially available, or can be readily prepared from L-tartaric acid.[5] This was converted into the bis(mesylate) **4** which subsequently gave the bis(azide) **5** via double substitution with inversion of configuration. Reduction to the bis(amine) **6** could be accomplished efficiently without removal of the benzyl groups, and this was followed by conversion into the bis(carbamate) **7**. This material could be converted into **9** (via **8**) by catalytic hydrogenation followed by treatment with base to induce double ring closure. Alternatively, **8** could be converted directly into **10** by the convenient method of Blechert[6] (Scheme 2). This straightforward route delivered crystalline **10** in 31% overall yield based on **3**, with no chromatographic purification being required. Compound **9** could also be acylated in the presence of base to give **10** (see Experimental).

*Attempted alkylation and aldol reactions of enolates derived from* **10**. With an efficient route to **10** in hand, we sought to transform the bis(imide) into the corresponding bis(enolate) species which was to be used in 'double' asymmetric alkylation and aldol reactions. However, despite extensive experimentation, all our efforts to achieve this proved fruitless, and our unsuccessful attempts are summarised in Fig. 2. In most cases the starting material was recovered, but sometimes decomposition (via hydrolysis at the exocyclic carbonyl groups) of the bis(imide) was also observed.

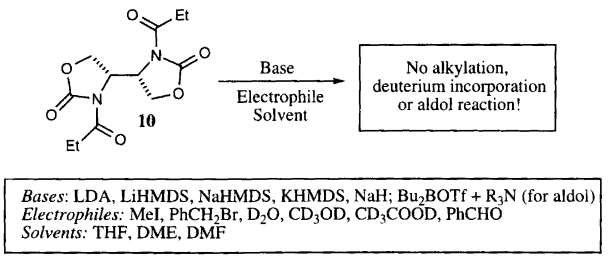



*Fig. 2.* Summary of unsuccessful attempts to react deprotonated **10**.

We hasten to add that we had no difficulty in reproducing the results of Evans[1f,g] using his chiral oxazolidinones as auxiliaries for asymmetric alkylation and aldol reactions. These experiments were carried out by the same investigator, using the same batches of base, solvent and electrophiles used in the corresponding but unsuccessful attempts with **10**.

*Detailed structural investigation of* **10**. In view of the recalcitrant nature of **10**, we decided to study its structure in more detail. At this point, although we were confident of the structure of **10** on the basis of the method of

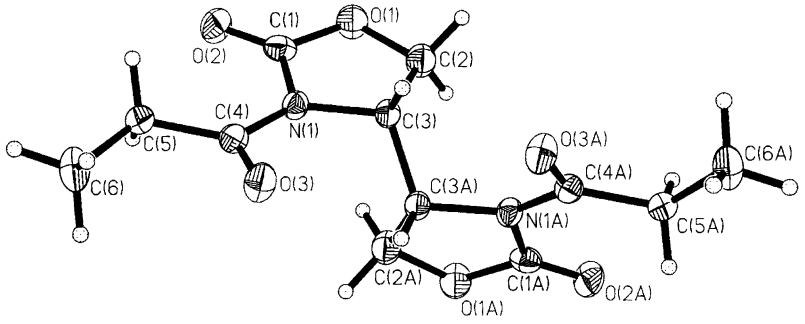



*Fig. 3.* Crystal structure of **10**.

synthesis as well as its NMR spectroscopic data (see the Experimental) we decided to perform an X-ray crystallographic analysis (see the Experimental). The results are shown in Fig. 3, and fully confirm the proposed gross structure.

The labelling of the atoms is as shown in Fig. 3. The molecule does indeed possess twofold symmetry, with the $C_2$-axis bisecting the central C(3)–C(3A) bond. Bond lengths and bond angles are listed in Table 3, and are in agreement with those found in similar compounds. The oxazolidinone rings are non-planar, with a twist conformation, and the torsion angles C(5)–C(4)–N(1)–C(1) and C(5)–C(4)–N(1)–C(3) are 10.6(4) and 172.7(2)°, respectively. On the whole, the structure does not provide any unpleasant surprises, and the relative alignment of the endo- and exo-cyclic carbonyl groups in each half of the molecule is what would be expected. In this conformation, there is an absence of $A^{1,3}$ strain[7] between the propionyl ethyl group and the substituent at C(3).

To investigate the conformational and electronic properties of **10**, we carried out a computational study[8–10] in which, for comparison, we included calculations on the corresponding imide **11** derived from the Evans oxazolidinone **1**. Monte Carlo simulations using the MM3$^+$ force field in MacroModel version 6.0 were performed for both **10** and **11**. The global energy minimum found for **10** (Fig. 4) is in good agreement with the structure found in the X-ray analysis (e.g. the torsion angle between the two methine hydrogen atoms is 46° in the experimental structure and 41° in the calculated one). In Fig. 5 is shown a superimposition of the global energy minima for **10** and **11**.

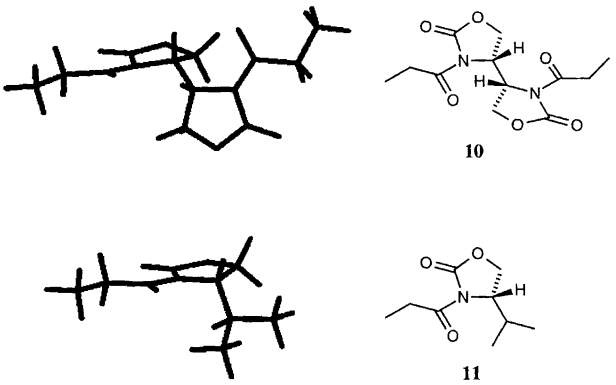



*Fig. 4.* Calculated global energy minima for **10** and **11**.

In order to investigate whether the difference in reactivity between **10** and **11** lay in an unexpected difference in ease of deprotonation, the respective global energy minima were geometry-optimized at the PM3 level and the electrostatic potential and charges were calculated using the same method. However, these calculations showed that the charges at the hydrogen atoms and the electrostatic potential at C(5) are the same in both compounds. Deprotonation by bases such as LDA or LiHMDS would thus be expected to be facile for both imides. Assuming that the enolate of **10** is formed, its lack of reactivity with external electrophiles could be explained on the basis of an intramolecular reaction with the exocyclic carbonyl of the other imide unit (Scheme 3). This would effectively 'tie up' both reactive centres of the molecule, and upon work-up adduct **12** would collapse either via a retro-aldol reaction or via C–N bond cleavage.

This possibility had been considered at the outset of the project, but we had reasoned that the second deprotonation or an intermolecular reaction with a good external electrophile such as benzyl bromide or benzaldehyde would be faster. However, this was obviously (and unfortunately!) not the case. The results of a conformational search involving rotation about the C(3)–C(3A) bond of **10** are shown in Fig. 6.

A conformer with a dihedral angle of $-167°$ between the two methine hydrogens was found, somewhat surprisingly, to lie only 1.2 kcal mol$^{-1}$ above the global minimum, from which it is separated by a barrier of ca.

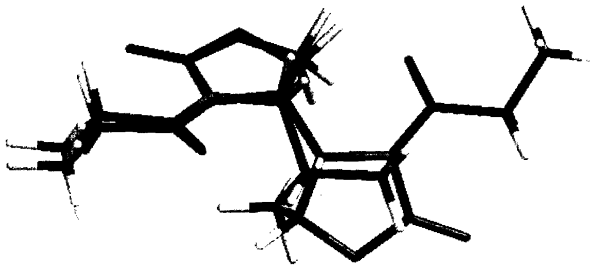
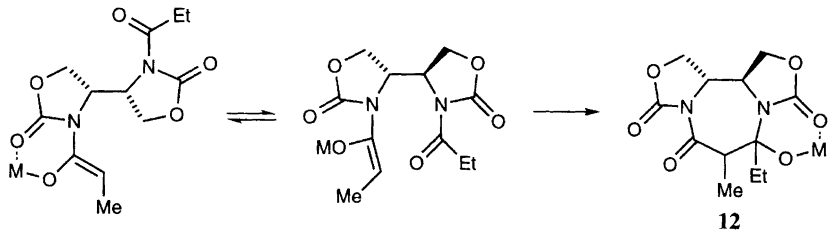


*Fig. 5.* Superimposition of calculated global energy minima for **10** and **11**.




*Scheme 3.* Proposed intramolecular reaction of the mono(enolate) of **10**.

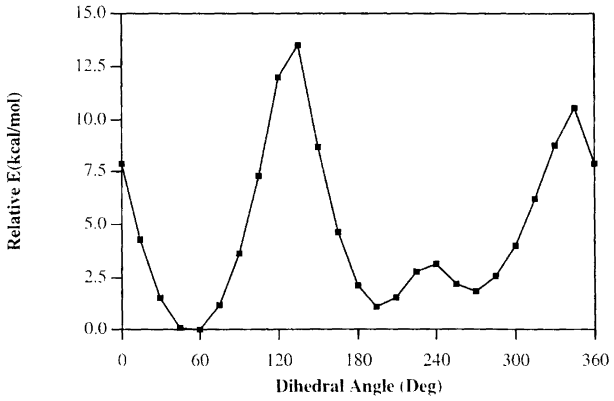



*Fig. 6.* Conformational search involving rotation about the C(3)–C(3A) bond of **10**.

10 kcal mol$^{-1}$. If these results are extrapolated to the mono(enolate) of **10**, then the undesired intramolecular reaction shown in Scheme 3 could occur without much difficulty. The following quotation from Robert Burns admirably sums up our thoughts at the end of this project: "The best laid plans o' mice an' men gang aft agley."

## Experimental

*General remarks.* $^1$H (200, 250 or 500 MHz) and $^{13}$C (50, 62.5 or 125 MHz) NMR spectra were recorded on a Bruker AC-200, a Bruker AC-250 or a Bruker AM-500 spectrometer ($CDCl_3$–TMS unless stated otherwise). Coupling constants, *J*, are given in Hz. IR spectra were obtained for neat samples on a Perkin–Elmer 1600 FT-IR instrument, and only the strongest/structurally most important peaks ($\nu_{max}$/cm$^{-1}$) are listed. Specific rotation values were measured at 25 °C on a Perkin–Elmer 241 polarimeter. Routine mass spectra were obtained on a VG Trio-2 instrument. Elemental analyses were performed at the Analytical Department of the Research Institute for Pharmacy and Biochemistry, Prague, Czech Republic. Pyridine was dried over calcium hydride and distilled under nitrogen. Dimethylformamide (DMF) was distilled at reduced pressure from calcium hydride. Methanol was distilled before use. 1,2-Dimethoxyethane (DME) was distilled under nitrogen from Na–benzophenone. Silica gel for flash chromatography was purchased from Grace-Amicon. Unless stated otherwise, reactions were carried out under an atmosphere of argon, in glassware which had been dried by being heated under vacuum with a heat-gun.

*Bis(mesylate)* **4**. Methanesulfonyl chloride (10.0 ml, 14.8 g, 129 mmol) was added dropwise to a stirred and cooled (ice bath) solution of **3** (13.6 g, 45 mmol) in dry pyridine (30 ml). The reaction mixture was stirred for 2 h (while the ice was allowed to melt) then poured into ethyl acetate (100 ml). The solution was extracted with ice-cold 1 M HCl (3 × 100 ml), saturated aqueous sodium bicarbonate (3 × 100 ml) and brine (100 ml). The organic phase was dried over $MgSO_4$ and evaporated to dryness to afford the crude bis(mesylate) as a colourless oil (19.6 g, 95%) which gradually turned yellow upon standing. The colourless material was NMR-spectroscopically pure and was used directly in the next step. $^1$H NMR: δ 7.45–7.42 (10 H, m), 5.00 (2 H, m), 4.60–4.45 (4 H, AB m, *J* 11.5), 3.78 (4 H, m), 3.03 (6 H, s). $^{13}$C NMR: δ 136.8, 128.5, 128.0, 127.9, 78.6, 76.3, 68.5, 38.7.

*Bis(azide)* **5**. The crude product from above (19.5 g, 43 mmol) was dissolved with stirring in dry DMF (100 ml) and $NaN_3$ (15.7 g, 241 mmol) was added. The mixture was stirred and heated at 100 °C for 16 h and then cooled to room temperature before being poured into water (800 ml). The mixture was extracted with ethyl acetate (7 × 100 ml) and the combined extracts were washed with water (4 × 200 ml) and brine (200 ml). The organic phase was dried over $MgSO_4$ and the solvent was removed without heating on a rotary evaporator. The last traces of solvent were removed by high vacuum pumping, and the desired product was obtained as a colourless oil (14.1 g, 93%) which was sufficiently pure for the next step. $[\alpha]_D$ −76 (*c* 0.85, $CHCl_3$). $^1$H NMR: δ 7.43–7.30 (10 H, m), 4.55 (4 H, s), 3.78–3.70 (2 H, m), 3.69–3.63 (4 H, m). $^{13}$C NMR: δ 137.4, 128.6, 128.0, 127.8, 73.6, 69.6, 61.0. IR: 2150 cm$^{-1}$ (vs). Anal. $C_{18}H_{20}N_6O_2$: C, H, N.

*Bis(amine)* **6**. Palladium-on-carbon (10% Pd, 5 g) was slurried in methanol (50 ml) and a solution of the bis(azide) from above (14 g, 39 mmol) in methanol (200 ml) was added. The resultant mixture was stirred under an atmosphere of hydrogen (balloon) for 18 h. The catalyst was carefully filtered off through Celite and a small portion of the filtrate was evaporated to dryness to provide a sample of the bis(amine) for spectroscopic characterisation. $^1$H NMR: δ 7.40–7.29 (10 H, m), 4.50

(4 H, s), 3.55–3.40 (4 H, m), 3.02 (2 H, br m), 1.79 (4 H, br m). $^{13}$C NMR: δ 138.1, 128.3, 128.0, 127.6, 73.4, 73.2, 52.5.

*Bis(carbamate)* **7**. The remainder of the filtrate from above was cooled in an ice bath and NaOH pellets (8.15 g, 204 mmol) were added. Methyl chloroformate (15.0 ml, 19.4 g, 202 mmol) was then carefully added dropwise (vigorous reaction) and the resultant mixture was stirred at room temperature for 2 h. The solution was concentrated to a volume of ca. 75 ml and water (200 ml) was added. The mixture was extracted with ethyl acetate (2 × 100 ml) and the combined extracts were washed with brine (100 ml). The organic phase was dried over $MgSO_4$ and evaporated to dryness to give a solid residue which was recrystallised from chloroform–hexane to give crystalline **7**, m.p. 79–80 °C (11.9 g, 73% based on **5**). $[\alpha]_D$ −33 (*c* 0.93, $CHCl_3$). $^1$H NMR: δ 7.40–7.24 (10 H, m), 5.38 (2 H, br), 4.51–4.36 (4 H, AB m, *J* 12), 4.03 (2 H, br m), 3.64 (6 H, s), 3.52–3.48 (4 H, m). $^{13}$C NMR: δ 157.3, 137.7, 128.5, 127.8, 127.7, 73.4 (two signals), 69.4, 52.3. IR: 3300 (br), 3100–2800 (s), 1700 (br s), 1560 (br s) cm$^{-1}$. MS (CI): *m/z* 417 $(M+H)^+$ (100%). Anal. $C_{22}H_{28}N_2O_6$: C, H, N.

*Diol* **8**. Compound **7** (9.83 g, 23.6 mmol) was dissolved in methanol (100 ml) and palladium hydroxide-on-carbon (1.16 g) was added. The resultant mixture was placed under an atmosphere of hydrogen (balloon) and stirred for 7 h at room temperature. At this point, $^1$H NMR spectroscopic analysis of an aliquot of the reaction mixture revealed that the reaction was incomplete. A second portion of the catalyst (1.03 g) was added and the mixture stirred under hydrogen for a further 7 h. The catalyst was removed by careful filtration through Celite, and the filtrate was evaporated to dryness. The residue was placed under high vacuum for 6 h before spectroscopic characterisation. There were obtained 4.57 g (95%) of the diol as a colourless oil. $^1$H NMR ($CD_3OD$): δ 4.90 (4 H, br s), 3.90–3.80 (2 H, m), 3.65 (6 H, s), 3.59–3.53 (4 H, m). $^{13}$C NMR ($CD_3OD$): δ 160.7, 63.7, 55.6, 53.7.

*Bis(oxazolidinone)* **9**. Diol **8** (106 mg, 0.52 mmol) was dissolved with stirring in dry DME (20 ml; the diol is not very soluble in common organic solvents) and a 60% suspension of NaH in mineral oil (76 mg, 1.8 mmol) was added. The mixture was heated to reflux overnight, cooled, and neutralised by addition of Amberlite IRC-50 ion-exchange resin. The mixture was filtered and the filtrate evaporated to dryness to give a residue which was partitioned between chloroform and water. The layers were separated and evaporated to dryness. None of the desired compound was obtained from the chloroform phase, while the aqueous phase yielded a solid which was rescrystallised from 95% ethanol. This provided **9** (81 mg, 91%) as a crystalline solid which decomposed at 265 °C. $[\alpha]_D$ −72 (*c* 1.06, $H_2O$). $^1$H NMR ($D_2O$): δ 4.65 (2 H, app. t, *J* 8.5), 4.33 (2 H, dd, *J* 8.5, 3.5), 4.19 (2 H, m), 3.70 (2 H, br m). $^{13}$C NMR ($D_2O$): δ 164.5, 70.2, 57.0. IR: 3300 (s), 2950 (w), 2850 (w), 1740 (vs, with shoulders at 1750 and 1780) cm$^{-1}$. MS: *m/z* 86 [100%; $M^+$ (172) not observed]. Anal. $C_6H_8N_2O_4$: C, H, N.

*Bis(oxazolidinone)* **10**. Diol **8** (4.5 g, 22 mmol) was suspended in dry DME (150 ml) and sodium hydride (55% suspension in mineral oil, 7.01 g, 160 mmol) was added. The mixture was heated at 100 °C for 20 h and cooled to room temperature before addition of propionyl chloride (8.25 ml, 8.75 g, 95 mmol). The resultant mixture was then heated at 80 °C for 48 h and cooled to room temperature before addition of acetic acid (8 ml). The

*Table 1.* Crystal and experimental data.

| | |
|---|---|
| Formula | $C_{12}H_{16}N_2O_6$ |
| Formula weight | 284.27 |
| Crystal system | Orthorhombic |
| Space group | $P2_12_12_1$ |
| Unit-cell dimensions: | |
| *a*/Å | 13.574(4) |
| *b*/Å | 8.584(3) |
| *c*/Å | 5.429(2) |
| Unit-cell volume, *V*/Å$^3$ | 632.6(4) |
| Formula units per unit cell, *Z* | 2 |
| *F*(000) | 300 |
| Calculated density, $D_x$/g cm$^{-3}$ | 1.492 |
| Radiation | Mo Kα |
| Wavelength, λ/Å | 0.710 73 |
| Linear absorption coefficient/mm$^{-1}$ | 0.121 |
| *T*/K | 160 |
| Crystal description | Colourless |
| Crystal size/mm | 0.08 × 0.08 × 0.26 |
| Diffractometer | Enraf–Nonius CAD-4F |
| Unit-cell determination: | |
| No. of reflections used | 25 |
| θ-range/° | 4.7–11.4 |
| Intensity data collection: | |
| $\theta_{max}$/° | 26.96 |
| Range of *h* | −17–17 |
| Range of *k* | 0–10 |
| Range of *l* | 0–6 |
| Scan mode | ω |
| Scan range, Δω | 1.10 + 0.45 tan θ |
| Total number of unique reflections | 1372 |
| No of independent reflections [$I > 2\sigma(I)$] | 1028 |
| Corrections | Lorenz and polarization |
| Structure refinement: | |
| Minimization of | $\Sigma w(\|F_o\|^2-\|F_c\|^2)^2$ |
| Anisotropic thermal parameters | All non-hydrogen atoms |
| Isotropic thermal parameters | Hydrogen atoms |
| No. of refined parameters | 123 |
| Weighting schemes | $[\sigma^2(F_o^2)+(0.0451P)^2+0.0000P]^{-1}$, $P=(F_o^2+2F_c^2)/3$ |
| $R=\Sigma\|\|F_o\|-\|F_c\|\|/\Sigma\|F_o\|$ | 0.0466 obs. data |
| $wR2=[\Sigma w\|F_o^2-F_c^2\|^2/\Sigma wF_o^4]^{1/2}$ | 0.0977 all data |
| $S=[[\Sigma w(\|F_o\|^2-\|F_c\|^2)^2/(N_{obs}-N_{var})]^{1/2}$ | 1.032 |
| Final $(\Delta/\sigma)_{max}$ | 0.045 |
| Final $\Delta\rho_{min}$ and $\Delta\rho_{max}$/e Å$^{-3}$ | −0.186 and 0.166 |

*Table 2.* Fractional atomic coordinates and equivalent isotropic thermal parameters (in Å$^2$).

| Atom | *x* | *y* | *z* | $U_{eq}$[a] |
|---|---|---|---|---|
| C(1) | 0.1433(2) | 0.2107(3) | 0.0030(5) | 0.0246(6) |
| C(2) | −0.0249(2) | 0.1780(4) | −0.0020(6) | 0.0297(7) |
| C(3) | 0.0152(2) | 0.0857(3) | −0.2204(5) | 0.0207(6) |
| C(4) | 0.1870(2) | 0.0550(3) | −0.3708(5) | 0.0215(6) |
| C(5) | 0.2940(2) | 0.0939(3) | −0.3473(6) | 0.0249(6) |
| C(6) | 0.3558(2) | 0.0178(4) | −0.5455(6) | 0.0338(7) |
| N(1) | 0.12220(13) | 0.1062(2) | −0.1855(4) | 0.0204(5) |
| O(1) | 0.05762(13) | 0.2562(2) | 0.1068(4) | 0.0331(5) |
| O(2) | 0.22164(13) | 0.2578(2) | 0.0688(4) | 0.0333(5) |
| O(3) | 0.15297(13) | −0.0165(2) | −0.5426(3) | 0.0289(5) |

[a] $U_{eq} = 1/3\,\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \boldsymbol{a}_i \cdot \boldsymbol{a}_j$.

*Table 3.* Bond lengths (in Å) and bond anbles (in °).[a]

| | |
|---|---|
| C(1)–O(2) | 1.192(3) |
| C(1)–O(1) | 1.350(3) |
| C(1)–N(1) | 1.391(3) |
| O(1)–C(2) | 1.434(3) |
| C(2)–C(3) | 1.526(4) |
| C(3)–N(1) | 1.475(3) |
| C(3)–C(3$^i$) | 1.529(5) |
| N(1)–C(4) | 1.406(3) |
| C(4)–O(3) | 1.208(3) |
| C(4)–C(5) | 1.496(3) |
| C(5)–C(6) | 1.513(4) |
| O(2)–C(1)–O(1) | 123.1(2) |
| O(2)–C(1)–N(1) | 128.5(2) |
| O(1)–C(1)–N(1) | 108.5(2) |
| C(1)–O(1)–C(2) | 111.4(2) |
| O(1)–C(2)–C(3) | 106.5(2) |
| N(1)–C(3)–C(2) | 101.0(2) |
| N(1)–C(3)–C(3$^i$) | 112.4(2) |
| C(2)–C(3)–C(3$^i$) | 113.8(2) |
| C(1)–N(1)–C(4) | 126.8(2) |
| C(1)–N(1)–C(3) | 111.9(2) |
| C(4)–N(1)–C(3) | 119.1(2) |
| O(3)–C(4)–N(1) | 118.2(2) |
| O(3)–C(4)–C(5) | 123.4(2) |
| N(1)–C(4)–C(5) | 118.5(2) |
| C(4)–C(5)–C(6) | 112.4(3) |

[a] Symmetry code $^i$: $-x, -y, z$.

mixture was poured into water (500 ml) and extracted with dichloromethane (3 × 125 ml). The combined extracts were dried over $MgSO_4$ and evaporated to dryness to give a solid residue which was recrystallised from chloroform–hexane. This yielded **10** as a crystalline solid (3.1 g, 50%) with m.p. 171–172 °C. $[\alpha]_D$ 104 (*c* 0.4, $CHCl_3$). $^1$H NMR ($CD_2Cl_2$): δ 5.00 (2 H, m), 4.38 (2 H, app. t, *J* 9.5), 4.32 (2 H, dd, *J* 9.5, 3.5), 2.94–2.81 (4 H, 2 × dq, *J* 16.5, 7), 1.13 (6 H, t, *J* 7). $^{13}$C NMR ($CDCl_3$): δ 174.5, 153.1, 64.3, 54.5, 29.0, 8.2. IR: 3000 (w), 2950 (w), 2850 (w), 1790 (vs), 1710 (s) cm$^{-1}$. MS: *m/z* 284 ($M^+$ 4%). Anal. $C_{12}H_{16}N_2O_6$: C, H, N.

*Conversion of* **9** *into* **10**. To a mixture of **9** (0.396 g, 2.30 mmol) and KI (0.112 g, 0.68 mmol) in dry DME (10 ml) was added NaH (55% suspension in mineral oil, 0.406 g, 9.3 mmol) and the resultant mixture was stirred at room temperature for 2 h. Freshly distilled propionyl chloride (1 ml, 1.06 g, 11.4 mmol) was added and the mixture was heated at 75 °C for 2 h. The mixture was cooled and quenched by addition of water (50 ml). The mixture was poured into dichloromethane (50 ml), the layers were separated and the aqueous phase was extracted with dichloromethane (50 ml). The combined organic phases were washed with water and dried over $MgSO_4$. Removal of the solvent gave a solid residue which was recrystallised from chloroform–hexane. This yielded **10**, identical in all respects with that described above (0.325 g, 50%).

*X-Ray crystallography.* Crystal and experimental data for compound **10** are listed in Table 1. The crystal was cooled to 160 K using the Cryostream nitrogen gas cooler system.[11] The unit cell was derived from least-squares fit refined diffractometer setting angles for 25 reflections. Four standards were measured for intensity and orientation control every 4 h. The intensities were corrected for Lorentz and polarization effects. The structure was solved by direct methods and refined by a full-matrix least squares technique. The non-hydrogen atoms were refined anisotropically. The hydrogen atoms were all located from electron-density maps and refined isotropically. The crystallographic computations were performed with SHELXS86[12] and SHELXL93.[13] The atomic scattering factors were taken from the literature.[14] The program SHELXTL[15] was used for illustration and PLATON[16] for molecular geometry calculations. The final positional parameters are listed in Table 2 and bond lengths and angles in Table 3.

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## References

1. For reviews of oxazolidinone auxiliaries, see: (a) Evans, D. A., Takacs, J. M., McGee, L. R., Ennis, M. D., Mathre, D. J. and Bertroli, J. *Pure Appl. Chem. 53* (1981) 1109; (b) Evans, D. A. *Aldrichim. Acta 15* (1982) 23; (c) Evans, D. A., Nelson, J. V. and Taber, T. R. *Top. Stereochem. 13* (1982) 1; (d) Ager, D. J., Prakash, J. and Schaad, D. R. *Chem. Rev. 96* (1996) 835; (e) Ager, D. J., Prakash, J. and Schaad, D. R. *Aldrichim. Acta 30* (1997) 3; (f) asymmetric aldol reaction: Evans, D. A., Bartroli, J. and Shih, T. L. *J. Am. Chem. Soc. 103* (1981) 2127; (g) asymmetric alkylation: Evans, D. A., Ennis, M. D. and Mathre, D. J. *J. Am. Chem. Soc. 104* (1982) 1737.
2. For an excellent example, see: Evans, D. A., Ratz, A. M., Huff, B. E. and Sheppard, G. S. *J. Am. Chem. Soc. 117* (1995) 3448.
3. See, e.g.: Davies, S. G., Evans, G. B. and Pearce, S. *Tetrahedron 50* (1994) 7521 and references therein.
4. Whitesell, J. K. *Chem. Rev. 89* (1989) 1581.
5. Mash, E. A., Nelson, K. A., Van Deusen, S. and Hemperly, S. B. *Org. Synth. 68* (1990) 92.
6. Huwe, C. M. and Blechert, S. *Tetrahedron Lett. 35* (1994) 9533.

7. Johnson, F. *Chem. Rev. 68* (1968) 375.
8. Molecular mechanics calculations: MM3$^+$ (MacroModel version 6.0): Mohamadi, F., Rickards, N. G. J., Guida, W. C., Liskamp, R., Lipton, M., Caufield, C., Chang, G., Hendrickson, T. and Still, W. C. *J. Comput. Chem. 11* (1990) 440.
9. MO calculations: PM3: Stewart, J. J. P. *J. Comput. Chem. 10* (1989) 209; Stewart, J. J. P. *J. Comput. Chem. 10* (1989) 221.
10. Spartan version 5.0.3 obtained from Wavefunction, Inc., 18401 Von Karman Avenue, Suite 370, Irvine, California 92715, USA.
11. Cosier, J. and Glazer, A. M. *J. Appl. Crystallogr. 19* (1986) 105.
12. Sheldrick, G. M. *Acta Crystallogr., Sect. A 46* (1990) 467.
13. Sheldrick, G. M. SHELXL93. *Program for Crystal Structure Refinement*, University of Göttingen, Germany 1993.
14. *International Tables for X-Ray Crystallography*, Kynoch Press, Birmingham 1974, Vol. IV. (Present distributor: Kluwer Academic Publishers, Dordrecht).
15. Sheldrick, G. M. SHELXTL95. Siemens Analytical X-ray Instruments Inc., Madison, WI 1995.
16. Spek, A. L. *Acta Crystallogr., Sect. A 46* (1990) C-34.

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